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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,937	08/21/2007	Anna Cederholm	EPCL:015US/ 10613209	6786

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EXAMINER	
WEN, SHARON X	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
03/31/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/599,937	CEDERHOLM ET AL.	
	Examiner	Art Unit	
	SHARON WEN	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6 and 8-13* is/are pending in the application.

4a) Of the above claim(s) *1,6,8,9 and 11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 01/20/2011, has been entered.

Claims 2 and 7 have been canceled.

Claim 4 has been amended.

Claims 1, 3-6, 8-13 are pending.

Claims 1, 6, 8, 9 and 11-13 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Election was made *without* traverse in the reply filed on 07/28/2009.

2. Regarding the currently amended claim 4, the following is noted:

Newly added claim limitations are directed to an invention encompassing species that are independent or distinct from the invention originally claimed for the following reasons:

The newly added claim limitations drawn to a dimmer of Annexin V and a PEG conjugate of Annexin V as the active ingredient in the claimed method of preventing plaque rupture were not previously claimed.

The Annexin V as originally presented in the examined claims and a dimmer of Annexin V and a PEG conjugate of Annexin V as recited in the amended claims are patentably distinct in structures, physiochemical properties and/or mode of action; and they do not share a common structure that is disclosed to be essential for common utility. Therefore, the method of preventing plaque rupture comprising administering these different molecules are also patentably distinct and would be subject to Restriction/Species Election requirement.

Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the claim recitation directed to a dimmer of Annexin V and a PEG conjugate of Annexin V are withdrawn from consideration as

being directed to a non-elected invention/species. See 37 C.F.R. 1.142(b) and M.P.E.P. 821.03.

3. Claims 3-5 and 10 are currently under examination as they read on a method of preventing plaque rupture in a subject comprising administering a composition comprising Annexin V.

4. This Action will be in response to Applicant's Arguments/Remarks, filed 12/02/2010.

The rejections of record can be found in the previous Office Action, mailed 09/02/2010.

Specification

5. Applicant's amendment to the specification, filed 12/02/2010, has been entered.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 4 and 10 are rejected under 35 U.S.C. 102(a)(e) as being anticipated by Blackenberg et al. (US 2003/0152513 A1, cited on IDS, see entire document).

Applicant's argument has been considered but has not been found convincing for reasons of record and reiterated below for Applicant's convenience:

> Blackenberg taught a method of preventing plaque rupture in a subject comprising administering annexin V (see, e.g., Abstract and Brief Summary of the Invention on pages 2 and 3). In particular, Blackenberg taught treating subject exhibiting vulnerable plaque which reads on preventing plaque rupture in the subject (see paragraph [0034]). Moreover, Blackenberg taught an effective amount of annexin V to be administered for therapeutic purpose (see paragraph [0031]).

Applicant argues that Blackenberg's teaching of using Annexin V as a "binding component" does not anticipate the present claims which recite the use of "native" Annexin V as the active component because Blackenberg's Annexin V is complexed to additional effector and targeting molecules thus can no longer be considered to be "native" Annexin V.

In response to Applicant's argument, it is first noted that the newly added limitation in the recitation of "native" Annexin V does not limit the Annexin V to be unconjugated. The instant specification does not provide any definition for "native" Annexin V. The only relevant decription found in the specification as-filed with regards to "native" Annexin V is found in the Abstract as follows:

> "The use of **native** Annexin V or an N-terminal fragment as an active component or a subfraction of immunoglobulins to manufacture a pharmaceutical composition is proposed to improve said binding."

Upon reading the above disclosure on "native" Annexin V, it is clear that the term "native" is intended to mean full length Annexin V. Blackenberg does not teach any Annexin V that is anything other than the full length protein. Therefore, the term "native" does not distinguish the claims from the prior art.

With regards to the argument on Annexin V being the active component, it is noted that Blackenberg taught that Annexin V itself has anti-apoptotic effects in vivo in addition to its inhibitory effects on membrane permeability to calcium, protein kinase C and phospholipase A2 in virto (see paragraph [0011]). Therefore, it cannot be ruled out that Annexin V in the conjugated complex as taught by Blackenberg does not play any active role preventing plaque rupture. Therefore, Applicant's argument in that Blackenberg's Annexin V is merely an inactive "binding component" is not convincing.

Therefore, the rejection is maintained as it applies to the amended claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blackenberg et al. (US 2003/0152513 A1, cited on IDS) in view of Manzi (Rheumatology 2000, 39:353-359).

Applicant's argument has been considered but has not been found convincing for reasons of record and reiterated below for Applicant's convenience:

> The teaching by Blackenberg has been discussed supra. Blackenberg did not teach that the subject is a SLE patient. However, it would have been obvious to one of ordinary skill in the art, at the time of the invention was made, to use annexin V to prevent plaque rupture in SLE patient because SLE patients are known to have a greater risk of plaque rupture as taught by Manzi (see entire document, in particular, see Endothelial cell injury on page 354 and Figure 1 on page 355). Therefore, one of ordinary skill in the art would have been motivated to use Annexin V to treat vulnerable plaque as taught by Blackenberg in SLE patients who are more susceptible to plaque rupture as taught by Manzi (see, e.g., Figure 1).
>
> Furthermore, one of ordinary skill in the art would also have been reasonably expected determine the effective amount of annexin V to administer in view of the teaching by Blackenberg that annexin V can be used for imagine diagnosis of vulnerable plaque by the treating physicians (see paragraph [0034]). Since the effective amount of Annexin V is a result effective variable which is related to the dosage range of the administration, the person of ordinary skill in the art would have been able to select an effective amount of annexin V by optimizing the dosage of annexin V based on the imagine diagnosis using labeled annexin V to bind endothelium in the subject.
>
> Therefore, the invention, as a whole, was prima facie obvious to one of ordinary skill in the art, at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's argument with regards to "native" Annexin V and Examiner's rebuttal are essentially the same as above.

In contrast to Applicant's assertion that there is no teaching or suggestion that Annexin V itself provides a biological activity, it is noted that Blackenberg taught that Annexin V itself has anti-apoptotic effects in vivo in addition to its inhibitory effects on membrane permeability to calcium, protein kinase C and phospholipase A2 in virto (see paragraph [0011]). Upon reading Balckenberg, one of ordinary skill in the art would not have been discouraged to use a full length Annexin V to prevent plaque rupture as taught by Blackenberg; nor would the ordinary artisan be surprised to find protective effect exerted by Annexin V. Therefore, Applicant's argument has not been convincing.

Therefore, the rejection is maintained as it applies to the amended claims.

Conclusion

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON WEN whose telephone number is (571)270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Huynh N. Phuong can be reached on (571)272-0846. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sharon Wen/
Primary Examiner, Art Unit 1644
March 27, 2011